UV-Induced DNA Self-Repair Mechanism Traced With Quantum Chemistry

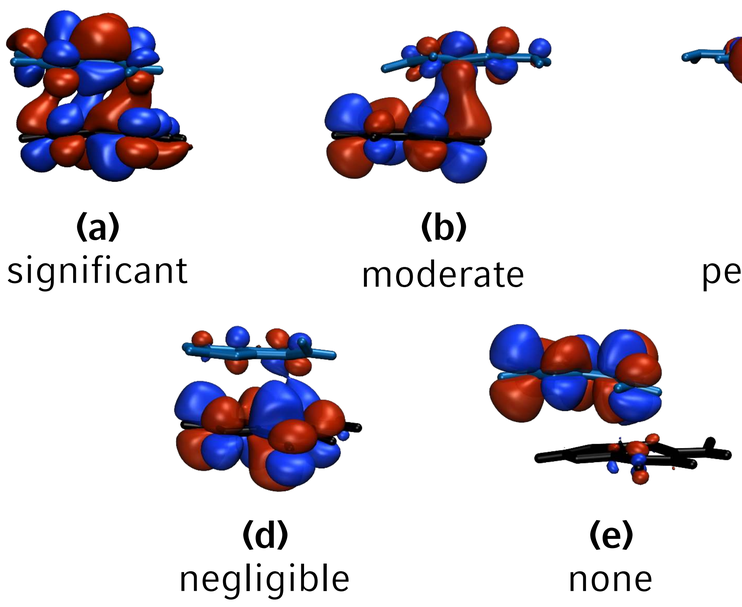
LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

Sebastian Reiter, Daniel Keefer, Vitus Besel and Regina de Vivie-Riedle

Abstract

- Specific DNA sequences promote self-repair of the cyclobutane pyrimidine dimer (CPD) photolesion[1] after UVB excitation (290nm)
- Theoretical investigations support photolyase-like repair mechanism

Classifying Orbital Overlap



Definition of Exciplexic Strength X_E

- Exciplex ➡ excitation into shared orbitals
- Excitation coefficients c from TD-DFT calculation
- State-specific: $X_{E,n} = \frac{\sum_{ab} c_{a,b}}{\sum_{abcde} c_{a,b,c,d,e}}$
- Averaged over N states: $X_E = \frac{1}{N} \sum_{n=1}^{N} X_{E,n}$ (here: $N = 5$)
- Takes values between 0 and 1

Step 2: G→A Charge-Transfer

CASSCF/cc-pVDZ

- Symmetric ππ* active spaces
- Orbital localization for easier interpretation
- Only G→A charge transfer in agreement with redox potentials[2] and experiment
- Excitation energies overestimated by 2–3eV (experiment: 4.28eV)

Excitation energies in eV and characters of excitations

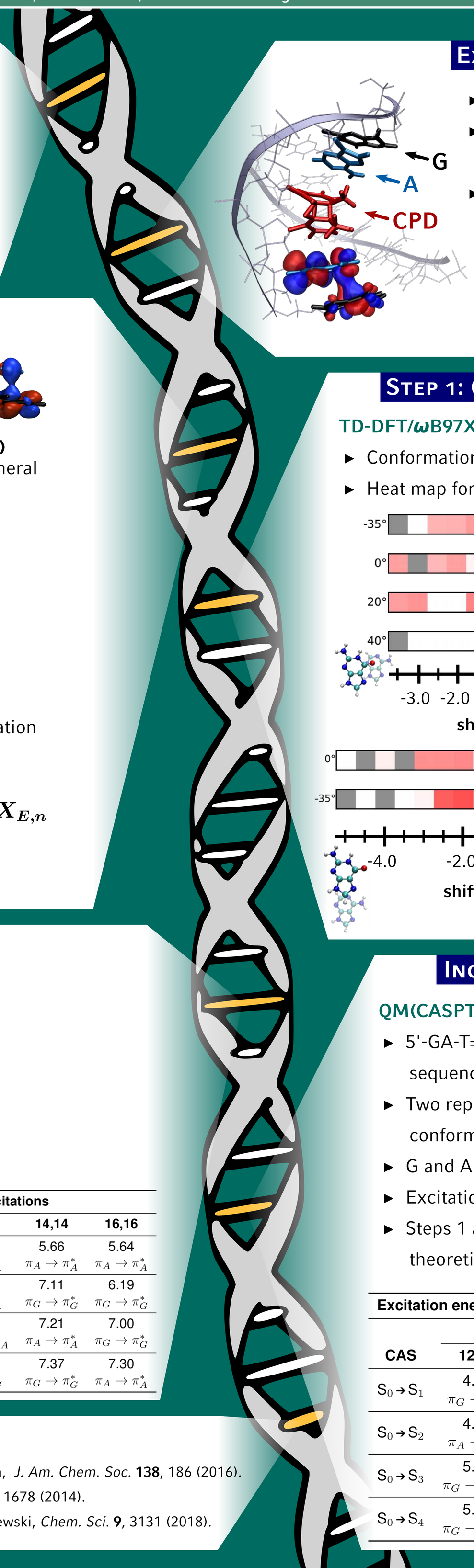
CAS	4,4	6,6	8,8	10,10	12,12	14,14	16,16
$S_0 \rightarrow S_1$	6.91 $\pi_G \rightarrow \pi_A^*$	6.57 $\pi_G \rightarrow \pi_G^*$	5.74 $\pi_A \rightarrow \pi_A^*$	6.46 $\pi_A \rightarrow \pi_A^*$	6.32 $\pi_A \rightarrow \pi_A^*$	5.66 $\pi_A \rightarrow \pi_A^*$	5.64 $\pi_A \rightarrow \pi_A^*$
$S_0 \rightarrow S_2$	7.27 $\pi_A \rightarrow \pi_A^*$	6.62 $\pi_G \rightarrow \pi_G^*$	6.60 $\pi_G \rightarrow \pi_G^*$	7.09 $\pi_A \rightarrow \pi_A^*$	7.08 $\pi_A \rightarrow \pi_A^*$	7.11 $\pi_G \rightarrow \pi_G^*$	6.19 $\pi_G \rightarrow \pi_G^*$
$S_0 \rightarrow S_3$	7.42 $\pi_G \rightarrow \pi_A^*$	7.20 $\pi_G \rightarrow \pi_A^*$	7.18 $\pi_A \rightarrow \pi_A^*$	7.21 $\pi_A \rightarrow \pi_A^*$	7.18 $\pi_G \rightarrow \pi_{G/A}^*$	7.21 $\pi_A \rightarrow \pi_A^*$	7.00 $\pi_G \rightarrow \pi_G^*$
$S_0 \rightarrow S_4$	7.63 $\pi_A \rightarrow \pi_A^*$	7.41 $\pi_G \rightarrow \pi_A^*$	7.63 $\pi_G \rightarrow \pi_A^*$	7.38 $\pi_G \rightarrow \pi_G^*$	7.37 $\pi_G \rightarrow \pi_G^*$	7.37 $\pi_G \rightarrow \pi_G^*$	7.30 $\pi_A \rightarrow \pi_A^*$

References

[1] D. B. Bucher, C. L. Kufner, A. Schlueter, T. Carell, W. Zinth, *J. Am. Chem. Soc.* **138**, 186 (2016).

[2] K. Lewis, K. Copeland, G. Hill, *Int. J. Quantum Chem.* **114**, 1678 (2014).

[3] R. Szabla, H. Kruse, P. Stadlbauer, J. Šponerb, A. L. Sobolewski, *Chem. Sci.* **9**, 3131 (2018).



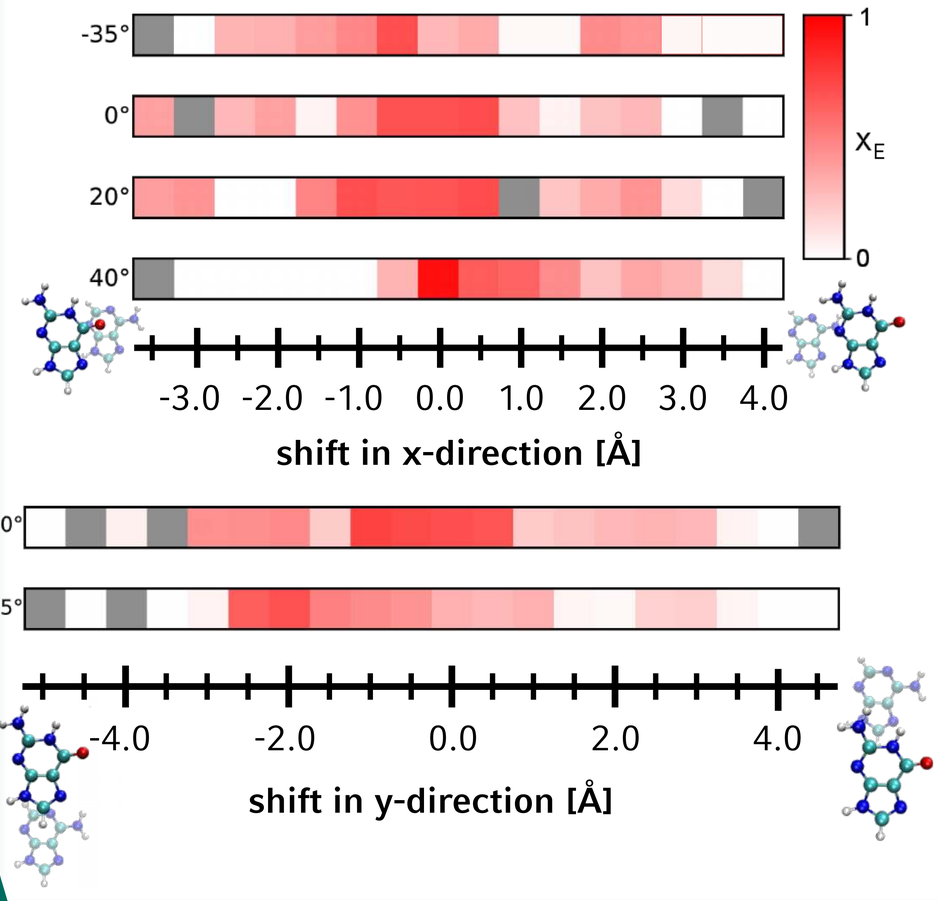
Experimental Background

- DNA sequence: 5'-GA-T=T-AG-3'
- Selective excitation at G, not at A, induces CPD self-repair
- Proposed mechanism[1]
  1. **(GA)* exciplex formation**
  2. **G→A electron transfer**
  3. $A^- \rightarrow$T=T electron injection
  4. CPD ring opening reaction

Step 1: (GA)* Exciplex Formation

TD-DFT/ωB97X-D/cc-pVDZ

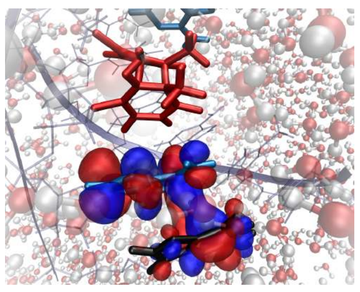
- Conformational scans of isolated G-A system
- Heat map for X_E of different structures



Including the Environment

QM(CASPT2)/MM//cc-pVDZ

- 5'-GA-T=T-AG-3' sequence in water
- Two representative conformations
- G and A in QM region
- Excitation energies in experimental range
- Steps 1 and 2 of the proposed mechanism theoretically validated



Excitation energies in eV and characters of excitations

	geometry 1		geometry 2	
CAS	12,11	14,13	12,11	14,13
$S_0 \rightarrow S_1$	4.40 $\pi_G \rightarrow \pi_G^*$	4.73 $\pi_G \rightarrow \pi_G^*$	4.47 $\pi_G \rightarrow \pi_G^*$	4.16 $\pi_G \rightarrow \pi_G^*$
$S_0 \rightarrow S_2$	4.93 $\pi_A \rightarrow \pi_A^*$	5.00 $\pi_G \rightarrow \pi_G^*$	5.49 $\pi_A \rightarrow \pi_A^*$	5.03 $\pi_A \rightarrow \pi_A^*$
$S_0 \rightarrow S_3$	5.22 $\pi_G \rightarrow Ry_A^*$	5.59 $lp_G \rightarrow \pi_G^*$	6.05 $\pi_A \rightarrow \pi_A^*$	5.87 $\pi_A \rightarrow \pi_A^*$
$S_0 \rightarrow S_4$	5.67 $\pi_G \rightarrow Ry_A^*$	5.70 $\pi_G \rightarrow \pi_A^*$	6.41 $\pi_G \rightarrow \pi_A^*$	6.02 $lp_G \rightarrow \pi_G^*$